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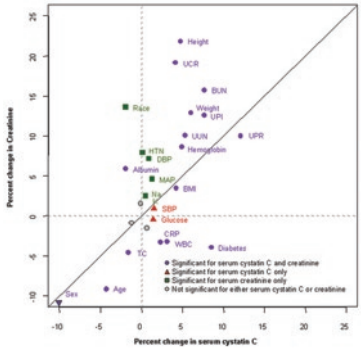
Cystatin C and GFR

The search for the best measurement of glomerular filtration rate (GFR) in epidemiological studies seems to be inexhaustible. After serum creatinine was battered by large studies that have raised questions about its utility, the appearance of cystatin C seems to have solved some of the problems. In a new study, Stevens *et al.* show associations between cystatin C and a number of lifestyle factors. The authors performed a cross-sectional analysis of more than 3000 clinical trial participants with chronic kidney disease in which both creatinine and cystatin C levels were measured as well as other clinical and routine laboratory parameters. Clearances of ^{125}I-iothalamate and ^{51}Cr-EDTA were also measured as an estimate of GFR. Cystatin C as a measure of GFR was affected by age and sex; it was lower in women and as age advanced. Further, diabetes caused an apparent increase in cystatin C. Higher C-reactive protein, higher white blood cell count, and lower serum albumin were associated with higher levels of cystatin C and lower levels of creatinine. Adjustments for age, sex, and race had a greater effect on the association of factors with creatinine than cystatin C. These results raise the same questions that have plagued the use of serum creatinine to estimate GFR measurements. **See page 652.**



Bisphosphonates in uremic vascular calcification

Bisphosphonates are now widely used for the prevention of uremic vascular medial calcification. But whether they act on the blood vessels directly or on alteration of mineral metabolism and bone resorption is not known. Lomashvili *et al.* address this question. They induced uremia by administering adenine to rats, which developed vascular calcification when fed a high-phosphorous diet. Daily administration of either of two bisphosphonates (etidronate or pamidronate) prevented aortic calcification and reduced bone formation, while bone resorption was not significantly affected. The authors then tested the effect of the medications on calcification of rat aortas *in vitro* and found that these agents inhibited calcification in culture and arrested further calcification of precalcified rats. It is now clear that calcification in the aortas occurs because the smooth muscle cells begin to express osteogenic proteins that play a large part in mediating this calcification. Importantly, bisphosphonates did not affect the expression of these osteogenic factors or calcification inhibitors *in vitro*. The fact that these drugs can inhibit both uremic vascular calcification and bone mineralization (each of them apparently directly) suggests that they act on a mechanism of calcification common to both of them. One possible result is the prevention of hydroxyapatite formation. Thus, bisphosphonates may not prevent vascular calcification without inhibiting bone formation in uremic rats. **See page 617.**

Vitamin D supplementation in renal transplant recipients

There is increasing evidence that vitamin D is important for aspects of cellular metabolism other than mineral metabolism, and that it has numerous beneficial effects. Now, the regulation of its plasma levels has acquired added significance. Specifically, serum levels of 25-hydroxy vitamin D were found to be frequently low following renal transplantation, the cause of which remains to be determined. In findings published in this issue, Courbebaisse *et al.* examine the possibility of increasing 25-hydroxy vitamin D in transplant recipients to bring the hormone levels closer to the normal range. The authors administered cholecalciferol every 2 weeks for 2 months, followed by a dose every other month, to renal transplant recipients who had low vitamin D levels. After the initial phase, serum 25-hydroxy vitamin D levels were normalized, serum calcium levels normalized, and serum parathyroid hormone levels decreased in most patients. Serum 25-hydroxy vitamin D levels decreased after the initial intensive phase but remained higher in patients who received cholecalciferol compared with those who did not. These studies show that it is possible to raise levels of vitamin D, which will prevent metabolic anomalies that result from low vitamin D in transplant patients. Although the reason these patients have low vitamin D levels remains unknown, immunosuppression therapy may play a role. **See page 646.**